

Meeting abstract

Open Access

The role of P2X₇ ATP receptors in the nervous system: potential implications in inflammatory and depression-like diseases

Cecília Csölle*, Rómeó D Andó, Mária Baranyi, József Haller and Beáta Spelágh

Address: Department of Molecular Pharmacology, Institute of Experimental Medicine, Hungarian Academy of Sciences, 1083 Budapest, Hungary

Email: Cecília Csölle* - csolle@koki.hu

* Corresponding author

from 15th Scientific Symposium of the Austrian Pharmacological Society (APHAR) Joint meeting with the Hungarian Society of Experimental and Clinical Pharmacology (MFT) and the Slovenian Pharmacological Society (SDF)
Graz, Austria. 19-21 November 2009

Published: 12 November 2009

BMC Pharmacology 2009, 9(Suppl 2):A53 doi:10.1186/1471-2210-9-S2-A53

This abstract is available from: <http://www.biomedcentral.com/1471-2210/9/S2/A53>

© 2009 Csölle and Spelágh; licensee BioMed Central Ltd.

Background

The P2X₇ receptor is a ligand-gated ion channel expressed in neuronal, glial and immune cells and is implicated in a wide range of pathological conditions, including ischemia, and inflammation. The P2X₇ receptor can modulate the maturation and release of the proinflammatory cytokine, interleukin-1 β (IL-1 β). IL-1 β is suggested to be involved in the pathophysiology of depression and sickness behaviour, elicited by peripherally administered bacterial lipopolysaccharide (LPS).

Methods

The levels of IL-1 β production were quantified in the hippocampi of rodents, using an ELISA kit. In order to identify genes involved in LPS-induced changes in P2X₇ receptor knock-out (KO) and wild-type (WT) mouse amygdala we performed whole mouse genome microarray analysis of mRNA extracted after six hours of intraperitoneal LPS injection.

Results

We showed that *in vivo* LPS challenge elevated IL-1 β levels in the rodent hippocampus. Antagonists of P2X receptors inhibited LPS-induced IL-1 β levels with a pharmacological profile similar to that of P2X₇ receptors and their inhibitory effect was attenuated in the absence of P2X₇ receptors. In WT mice, LPS overexpressed mRNA encoding P2X₄ and P2X₇ receptors in the hippocampus and also

caused a remarkable increase in the levels of IL-1 β in the blood serum. The hippocampal increase of IL-1 β was substantially alleviated when contamination by circulating blood cells was excluded by transcardial perfusion, indicating the peripheral origin of hippocampal IL-1 β elevation. Six h after i.p. injection of LPS, the expression of 74 transcripts (41 upregulated and 33 downregulated) was significantly altered two-fold or more in mouse amygdala. These genes can be classified according to their biological function as follows: inflammatory response: Il4ra, Ccl21b; depression-associated genes: Slc17a7, Nfatc1, Creb3l3. Our microarray studies have identified 8,165 transcripts that were significantly affected by the deficiency of P2X₇ receptors indicating that the deletion of P2X₇ receptors causes genome-wide alterations of gene expression including depression-related genes in mouse amygdala (GABA_A, GABA_C receptors, AMPA and NMDA_{2B} ionotropic and mGlu₅, mGlu₇ metabotropic glutamate receptors were downregulated in KO mice).

Conclusion

These results point to the key role of the endogenous activation of P2X₇ receptors in the level of IL-1 β and in the regulation of individual protein which could be of potential interest for the study of the neurobiological basis underlying psychiatric diseases like depression.